Effect of ultraviolet germicidal lights installed in office ventilation systems on workers' health and wellbeing: double-blind multiple crossover trial

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Summary

Background Workers in modern office buildings frequently have unexplained work-related symptoms or combinations of symptoms. We assessed whether ultraviolet germicidal irradiation (UVGI) of drip pans and cooling coils within ventilation systems of office buildings would reduce microbial contamination, and thus occupants' work-related symptoms.

Methods We undertook a double blind, multiple crossover trial of 771 participants. In office buildings in Montreal, Canada, UVGI was alternately off for 12 weeks, then turned on for 4 weeks. We did this three times with UVGI on and three times with it off, for 48 consecutive weeks. Primary outcomes of self-reported work-related symptoms, and secondary outcomes of endotoxin and viable microbial concentrations in air and on surfaces, and other environmental covariates were measured six times.

Findings Operation of UVGI resulted in 99% (95% CI 67–100) reduction of microbial and endotoxin concentrations on irradiated surfaces within the ventilation systems. 771 participants appeared to remain masked, and reported no adverse effects. On the basis of within-person estimates, use of UVGI was associated with significantly fewer work-related symptoms overall (adjusted odds ratio 0·8 [95% CI 0·7–0·99]), as well as respiratory (0·6 [0·4–0·9]) and mucosal (0·7 [0·6–0·9]) symptoms than was non-use. Reduction of work-related mucosal symptoms was greatest among atopic workers (0·6 [0·5–0·8]), and never-smokers (0·7 [0·5–0·9]). With UVGI on, never-smokers also had large reduction of work-related respiratory (0·4 [0·2–0·9]), and musculoskeletal symptoms (0·5 [0·3–0·9]).

Interpretation Installation of UGVI in most North American offices could resolve work-related symptoms in about 4 million employees, caused by microbial contamination of heating, ventilation, and air-conditioning systems. The cost of UVGI installation could in the long run prove cost-effective compared with the yearly losses from absence because of building-related illness.

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Introduction

The office or office-like indoor environment is now the workplace for more than 70% of the work force in North America and western Europe.[1,2] Most of these people work in buildings with sealed exterior shells, in which highly automated heating, ventilation, and air conditioning systems, run by only one or two operators, control the indoor environment.[3] Many reports have documented health problems related to this work environment;[2–4] their resolution could result in health benefits for as many as 15 million workers, and economic benefits of $5–75 billion per year, in the USA alone.[2]

Most occurrences of illnesses in workers in these buildings, which are termed non-specific building-related illnesses[3] or symptoms[2], remain unexplained,[2,3] but evidence suggests that microbial contamination of building air-conditioning systems plays a part. Cross-sectional studies have consistently detected increased prevalence of such symptoms in workers in air-conditioned buildings.[5] Heavy growth of bacteria, fungi, and protozoa has been documented in air-cooling units,[6] air-conditioning cooling coils,[7,8] and drip pans[7,9] within office buildings. Microbial contamination has resulted in outbreaks of rhinitis, humidifier fever, asthma, hypersensitivity pneumonitis, and Pontiac fever.[8,10–14]

The effectiveness of ultraviolet germicidal irradiation (UVGI) lights in elimination of microbial contamination has been shown in many settings, although not in office buildings. After a pilot study to assess feasibility and safety,[7] we investigated whether use of UVGI lights in office ventilation systems would reduce surface microbial contamination and occupants' work-related symptoms.

Methods

Participants

We selected three office buildings in Montreal, with sealed windows, mechanical ventilation, and air conditioning, in which smoking was not allowed. In one building, the lower and upper halves had independent ventilation systems, and different corporate tenants; these were treated as two buildings, with independent operation of UVGI lights. No building had had an outbreak of building-related illness.

On a sample of floors within each building (total 14 floors), all full-time workers with a fixed worksite were eligible. They were approached for written informed consent, and their worksite locations marked on detailed floor plans. The research ethics committee of the Montreal Chest Institute of the McGill University Health Center approved this study.

On the basis of pilot study results,[7] 632 eligible participants were needed to detect a 10% reduction in reporting of work-related symptoms with an α of 0·05 and power of at least 90% based on two-sided tests.[15] This number was increased to 980, in case 20% did not participate, and 15% dropped out.

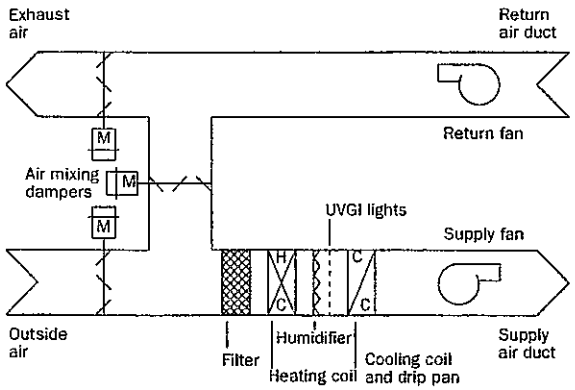

Figure 1: **Schematic diagram of a typical HVAC system**

Study design

We undertook a double-blind multiple cross-over trial from July 1, 1999, to July 31, 2000. UVGI lights directly irradiating the cooling coils and drip pans (figure 1) in the ventilation systems supplying the selected floors, were controlled experimentally. The lights were turned on for 4 consecutive weeks, or off for 12 consecutive weeks, which provided sufficient time to decontaminate and then recontaminate.[7] Other ventilation system functions—heating, cooling, humidification, and percentage recirculation—were operated as usual. In every building, UVGI lights were first off, then on for 4 weeks, then off for the next 12 weeks; this was repeated. The interventions were staggered, so that UVGI were on in only one building at any time.

The UVGI lamps (Sanuvox Technologies, Montreal, Canada) were of low-pressure (2·5 TORR) mercury-laden, argon-neon type, and incorporated a Getter assembly. The shell of the bulb consisted of pure fused quartz, coated with titanium oxide to avoid ozone production. Lamps had net output of 450 mW/cm^2 at 1 m distance in the 245–266 nm wavelength band, also coated with titanium oxide. The lamps were mounted with parabolic reflectors, 15–75 cm from the cooling coils and drip pans. For resistant organisms on the irradiated surfaces, the survival time was predicted to be less than 4 mins.

In the last week before UVGI was switched, participants completed self-administered questionnaires about demographic, personal, medical, and work characteristics, which had been developed and validated previously.[7,16–18] Every worker completed a maximum of six questionnaires (three with UVGI off, and three with it on). Workers reported whether or not they had ten specific symptoms before or after arrival at work on the same day. The symptoms elicited—headache, fatigue, concentration difficulties, irritation of skin, eyes, nose, or throat, nasal congestion, musculoskeletal (muscle, joint, or back pains), and respiratory (cough, chest tightness, or difficulty breathing)—were the most commonly reported previously.[3–5,19] Symptoms that began after arrival at work were regarded as work-related, and grouped as previously described:[4,18,19] mucosal (irritation of eyes, nose or throat, or nasal congestion) or systemic (headache, fatigue, or difficulty concentrating).

The participating workers, and personnel responsible for distribution and collection of questionnaires, were informed of the study objectives, but not whether the UVGI lamps were on or off. Effectiveness of masking was assessed from occupants' reports to building operators, and questionnaire responses for environmental satisfaction ratings, assessment of adequacy of the ventilation system, and any other comments.

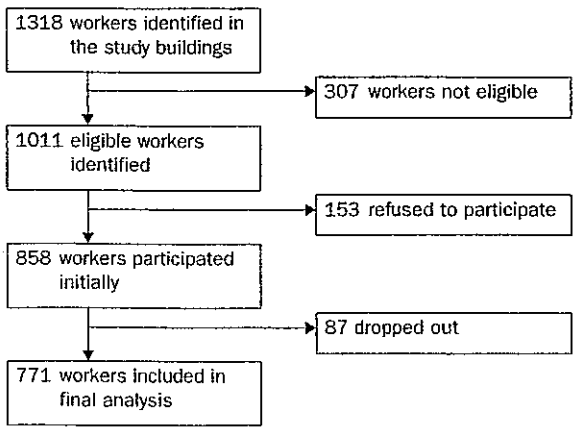

Figure 2: **Trial profile**

Measurements

In every building, environmental factors were measured in the same weeks as questionnaire collection. These measuresments were matched to participants' questionnaire responses according to building location, and ventilation system in their worksite. At four worksites per floor, airborne microbes were obtained from within ventilation systems and outdoor air by direct application of Petri dishes containing media for fungi or bacteria, with Burkhard volumetric air samplers operating at 12 L per min for 15 min (Burkhard Manufacturing, Hertfordshire, UK). Surface microbes were assessed with coupons—flat pieces of sheet metal measuring 5 cm×5 cm. These coupons were sterilised and, within every ventilation system, were placed on cooling coils and in drip pans (exposed to UVGI), and on filters (not exposed to UVGI). Four coupons were obtained from each location, and placed, UVGI-exposed side facing down, on culture media in Petri dishes.

	Non-participants (n=153)	Dropped out† (n=87)	Participants‡ (n=771)
Personal characteristics			
Age (years)	..	42·9 (10·5)	43·1(8·5)
Women	95 (62%)	41 (47%)	465 (60%)
French mother tongue	131 (86%)	68 (78%)	616 (80%)
Smoking (n=67)			
Never	..	28 (42%)	328 (45%)
Ex-smoker	..	22 (33%)	208 (28%)
Current smoker	..	17 (25%)	194 (27%)
Medical (n=45)			
Atopic illness	..	30 (45%)	308 (42%)
Other medical	..	15 (22%)	167 (23%)
Work characteristics			
Job type (n=67)			
Clerical	..	21 (31%)	275 (38%)
Manager	..	25 (37%)	288 (39%)
Professional	..	21 (31%)	168 (23%)
Years worked same employer	..	13·8 (10·9)	13·7 (9·6)
Hours worked at worksite per day	..	7·1 (1·6)	7·1 (1·9)
Hours worked on computer per day	..	4·9 (2·6)	5·4 (2·3)

Data are number (%) or mean (SD). *Five did not complete a baseline questionnaire, and 20 of those who dropped out never completed a baseline questionnaire. Additionally, responses to some items do not total up to the number of respondents because of missing responses on those items. †Some completed some questionnaires but not enough to analyse the effect of UVGI. ‡Some completed at least one symptom questionnaire with UVGI off, and one with UVGI on.

Table 1: **Characteristics of participants***

	UVGI off	UVGI on	Difference in means
Thermal conditions at worksites*			
Mean temperature over day (°C)	24·7 (1·7)	24·0 (1·4)	0·7 (0·5 to 0·9)
Mean relative humidity over day (%)	36% (13%)	32% (11%)	4% (2% to 6%)
Mean air velocity over day (m/sec)	0·90 (0·44)	0·90 (0·33)	0·0 (–0·05 to 0·06)
HVAC recirculation over day (%)	79% (4%)	82% (6%)	–2% (–4% to 0·4%)
Chemical parameters worksites†			
CO_2 peak value			
At worksites (ppm) in afternoon	619 (116)	609 (81)	10 (–4 to 25)
TVOCs			
At worksites (mcg/m³)	134 (83)	163 (126)	–29 (–84 to 26)
In outdoor air (mcg/m³)	69 (112)	157 (199)	–88 (–250 to 73)
Formaldehyde			
At worksites (ppm)	0·030 (0·033)	0·039 (0·045)	–0·019 (–0·029 to 0·011)
In outdoor air (ppm)	0·026 (0·032)	0·041 (0·073)	–0·015 (–0·062 to 0·031)
Ozone			
At worksites (ppb)	3·0 (3·6)	2·2 (2·0)	0·7 (–0·7 to 2·2)
In outdoor air (ppb)	8·8 (6·4)	11·1 (10·6)	–2·3 (–11·1 to 6·4)
Nitrogen oxides			
At worksites (μcg/m³)	41·9 (28·1)	38·1 (27·3)	3·8 (–10·5 to 18·1)
In outdoor air (μcg/m³)	52·8 (36·1)	62·9 (66·7)	–10·1 (64 to 43)

ppm=parts per million. HVAC=heating, ventilation, and air-conditioning. TVOC=total volatile organic compounds. ppb=parts per billion. Data are mean (SD) or mean difference (95% CI). *2400 measurements each for temperature, humidity, air velocity, and CO_2. †318 measurements each of TVOC, formaldehyde, ozone, and nitrogen oxides.

Table 2: **Environmental conditions: thermal and chemical**

	UVGI off	UVGI on	Difference in median values
Microbial indices*			
Fungi (total CFU from MEA and Sabouraud)			
HVAC surfaces			
Filters (cfu/coupon)	3 (1–16)	2 (0–8)	1 (–2 to 3)
Drip pans (cfu/coupon)	3 (1–13)	0 (0–0)	2 (1 to 6)
Cooling coils (cfu/coupon)	3–5 (0–19)	0 (0–0)	3 (2 to 5)
HVAC airborne			
Outdoor air (cfu/m³)	12 (0–36)	14 (0–43)	–3 (–19 to 12)
Return air (cfu/m³)	0 (0–8)	0 (0–17)	0 (0 to 0)
Supply air (cfu/m³)	0 (0–8)	0 (0–0)	0 (0 to 0)
Worksite airborne (cfu/m³)	0 (0)	0 (0–9)	0 (–9 to 0)
Bacteria (CFU from blood agar plates)			
HVAC surfaces			
Filters (cfu/coupon)	25 (5–50)	9–5 (3–18)	13 (4 to 23)
Drip pans (cfu/coupon)	14 (2–27)	1 (0–3)	13 (2 to 19)
Cooling coils (cfu/coupon)	15 (6–30)	0 (0–1)	15 (11 to 21)
HVAC airborne			
Outdoor air (cfu/m³)	50 (31–93)	68 (20–109)	–13 (–96 to 46)
Return air (cfu/m³)	15 (8–27)	17 (8–29)	–3 (–14 to 3)
Supply air (cfu/m³)	18 (9–60)	18 (8–38)	0 (–9 to 8)
Worksite airborne (cfu/m³)	127 (31–262)	92 (23–185)	19 (–93 to 135'
Endotoxin†			
Ventilation system surfaces (EU/coupon)			
Filters	17 (6–48)	21 (10–42)	–3 (–15 to 18)
Drip pans	32–5 (15–260)	3 (0–11)	29 (18 to 133)
Cooling coils	8.0 (0–24)	0 (0–8)	8 (1 to 12)
Airdrborne (eu/m³)			
Outdoor air	0·23 (0·05–0·28)	0·15 (0–0·35)	0·08 (–0·30 to 0·23)
Worksites	0 (0–0·07)	0 (0–0·08)	0 (–0·08 to 0·07)
Ventilation system			
Before filter	0·16 (0–0·33)	0·08 (0–0·18)	0·06 (–0·16 to 0·19)
After filters	0·07 (0–0·32)	0·0 (0–0·05)	0·06 (0 to 0·19)
After cooling coils	0·065 (0–0·14)	0·02 (0–0·18)	0·03 (–0·11 to 0·13)

cfu=colony-forming units. MEA=malt extract agar. EU=endotoxin units. *1240 measures each of bacteria and fungi. †284 samples assayed for endotoxin.

Table 3: **Environmental conditions: organisms**

All plates were incubated at 37°C for 48 h, to count total colony-forming units. A sample of these plates were cultured at 25°C for 1 week, then colony types were differentiated and counted with a stereomicroscope. Representative colonies were processed for species identification directly, or subinoculated onto appropriate agar media. Species were identified as described in appropriate identification manuals, and according to standard protocols.[20]

At the same locations as microbial samples, coupons were retrieved, and airborne samples for endotoxin measurements were captured on an isopore polycarbonate membrane (Millipore, Biccerica, MA, UK) backed by a glass fibre pad (Millipore) with a volumetric air pump. The pump was calibrated with an electronic bubble meter, operating at 2 L/min for 10 h per day, for 5 consecutive workdays. The exposed surface of every coupon was scraped with an endotoxin-free spatula followed by washing with 5 mL of 0·01% triethylamine 0·05 mol/L potassium phosphate, pH 7·5 (triethyl amine phosphate [TAP] buffer). The scrapings and washings were collected in an endotoxin-free borosilicate glass sample tube (baked at 270°C for a minimum of 30 min), then sonicated for 1 h at 25°C. Air samples were eluted in 5 mL of TAP buffer with bath sonication. All samples were analysed with the Limulus amoebocyte lysate assay following the KLARE protocol.[21] Samples for endotoxin measures were taken in the final 2 weeks of symptom measurement (May–July, 2000) only, and thus were repeated similarly in two additional trials with UVGI off and on, from August–December, 2000, and July–October, 2001.

In the morning and afternoon of 1 day, temperature, humidity, air velocity, and carbon dioxide (CO_2) were measured at eight worksites per floor and in the supply air (SA), return air (RA), and outdoor air (OA) of the ventilation systems. Measurements of temperature, humidity, and air velocity were done with a hot wire anemometer, and of carbon dioxide with a direct reading infrared non-dispersed detector. Percent recirculation was calculated as: $[(SACO_2–OACO_2)/(RACO_2–OACO_2)]\times100$.[18]

In the same weeks, four chemical contaminants were measured in outdoor air, ventilation systems, and one

	UVGI off		UVGI on		Difference in median values		Health effects associated	(REF)
	Coupons* with organism	Median cfu† (IQR)	Coupons* with organism	Median cfu† (IQR)	p	Mean (95% CI)		
Alternaria alternata	88%	10 (2–18)	25%	0 (0–1)	0·006	10 (2 to 2 1)	Asthma	(22; 58–60)
							Sinusitis	(57)
Cladosporium cladosporoides	88%	11 (9–16)	25%	0 (0–1)	0·003	11 (9 to 16)		
Yeasts	100%	9 (5–14)	50%	1 (0–3)	0·003	8 (3 to 13)		
Epicoccum nigrum	63%	7 (0–12)	12%	0 (0–0)	0·03	7 (0 to 13)	Sinusitis	(57)
Aureobasidium pullulans	50%	1 (0–3)	50%	1 (0–1)	0·4	1 (–1 to 3)	Hypersensitivity, Pneumonitis	(15)
							Humidifier, Fever	(19)
Penicillium spp	75%	3 (1–3)	0	0 (0–0)	0·004	3 (0 to 3)	Asthma	(8)
							Hypersensitivity, Pneumonitis	(8)
Aspergillus spp	25%	0 (0–1)	0	0 (0–0)	0·14	0 (0 to 1)	Hypersensitivity, Pneumoniti	(15)
							Respiratory symptoms	(65)
							Sinusitis	(57)

*With UVGI on only eight coupons were exposed—results from these eight and eight coupons from corresponding sites with UVGI off only are shown. †Mean CFU per coupon.

Table 4: **Organisms detected on surface samples (coupons) before and after UVGI exposure**

to two worksites per floor. Total volatile organic compounds were collected with activated charcoal tubes with volumetric air pumps operated at 300 mL/min over 8 h for 2 consecutive working days and analysed with the flame ionisation detection method (method 1501 modified[22]). Formaldehyde was collected over 24 h with SKC (Phica, PA, USA) passive samplers and analysed with ASTM method D5014–89.[23] Ozone was collected by bubbling air at 1 L/min over 8 h through ozone absorbency liquid, and analysed with NIOSH methods P and CAM 154.[22] Nitrogen oxides were obtained with SKC volumetric air samplers operating at 75 mL per min over 8 h on to a solid sorbent sampling tube containing a triethynolamine impregnated molecular surface and analysed using NIOSH method P and CAM 231.[22] Carbon monoxide, measured with a portable electro-chemical detector (Interscan model 1142, Interscan, Chatsworth CA, USA), and airborne dust, measured with a Grimm 1105 particle analyser (Grimm Technologies, Douglasville, GA, USA), were well below recommended limits at all worksites in the first 2 weeks, so were not measured subsequently.

Data analysis

The mean and 95% CIs for differences in median values of microbial indices (UVGI on *vs* off), which are judged to be indicators of the effectiveness of the experimental intervention, were estimated by bootstrapping.[24] p values for difference in median values were calculated with the Kruskal-Wallis non-parametric test. Mean and 95% CIs for differences, under the two experimental conditions, in thermal and chemical environmental indices, which are judged to be covariates in the design, were estimated with parametric tests.[15]

To take advantage of the repeated measures design, within-person statistical analyses were undertaken throughout. The unadjusted or crude estimate of effect was calculated with the odds ratio estimator for matched pairs.[25] This method estimated a summary odds ratio and 95% CI, as the ratio of workers who were symptomatic only with UVGI on, to those symptomatic only with UVGI on (on/off).[25]

The CIs calculated with this approach were independent, yet participants completed multiple questionnaires. Therefore, the CIs were also calculated by bootstrapping the ratio of the sum of the three on counts to the sum of the three off counts.[24] The bootstrapping unit used was all pairs of weeks when subjects' symptom status changed under the two UVGI conditions.

A second method to assess these CIs was to use the number of pairs of weeks when symptom status was different as the denominator, and the number when they had symptoms only with UVGI on as a binomial random variable. The binomial parameter of interest was p=OR/(1+OR). Using SAS macro GLIMMIX (version 8), we fitted a random effects binomial model to account for any over-dispersion in the odds ratios across individuals, and to thereby correct the variance of the overall log odds ratio for any such heterogeneity of the odds ratio.[26]

PROC GLIMMIX was also used to assess the heterogeneity of the odds ratio across the 14 floors within the buildings, and across the different buildings in a random effects binomial regression model (heterogeneity might indicate clustering of responses among workers

	Weeks 1 and 2		Weeks 3 and 4		Weeks 5 and 6		Overall			
	UVG1 off (746)	UVG1 on (636)	UVG1 off (608)	UVG1 on (593)	UVG1 off (587)	UVG1 on(515)	UVG1 off (1941)	UVG1 on (1744)	Difference in ratings OR (95% CI)	Mean (95% CI)
Is ventilation adequate today?										
Yes	67%	64%	64%	70%	71%	72%	67%	68%	1·04 (0·9–1·2)	
Environment Satisfaction Rating*										
Thermal†	1·2	1·2	1·4	1·2	1·2	1·0	1·2	1·3		0·07 (0·003 to 0·1)
Physical‡	0·8	0·8	0·7	0·8	0·8	0·7	0·8	0·8		0·02 (–0·03 to 0·07)
Indoor air quality§	1·6	1·7	1·9	1·9	2·0	2·0	1·8	1·9		–0·05 (–0·1 to 0·01)
Overall	1·2	1·2	1·3	1·3	1·3	1·3	1·3	1·3		0·01 (–0·03 to 0·05)

Data are mean (SD). *All ratings scored from 0 (ideal) to 4 (terrible). †Mean rating of temperature, humidity, and air movement. ‡Mean rating of lighting, noise, and work space. §Mean rating of odours, dust, and air quality.

Table 5: **Participants' assessment of environmental conditions**

	No symptoms either setting	Symptoms with both settings	Symptoms only with UVGI off	Symptoms only with UVGI on	Odds ratio for UVGI on:off
Work-related*					
Total for all trials†					
Any	614 (40%)	434 (28%)	283 (18%)	212 (14%)	0·74 (0·6–0·9)
Systemic	927 (60%)	171 (11%)	223 (14%)	222 (14%)	0·99 (0·8–1·2)
Mucosal	806 (52%)	301 (20%)	246 (16%)	190 (12%)	0·77 (0·6–0·9)
Respiratory	1429 (93%)	17 (1%)	56 (4%)	41 (3%)	0·73 (0·5–1·1)
Musculo-skeletal	1347 (88%)	37 (2%)	94 (6%)	65 (4%)	0·69 (0·5–0·9)
Before work					
Total for all trials†					
Any	887 (58%)	190 (12%)	205 (13%)	242 (16%)	1·18 (0·98–1·4)
Systemic	1306 (86%)	25 (2%)	86 (6%)	107 (7%)	1·24 (0·9–1·6)
Mucosal	1045 (69%)	113 (7%)	162 (11%)	204 (13%)	1·26 (1·03–1·5)
Respiratory	1415 (93%)	10 (1%)	47 (3%)	52 (3%)	1·11 (0·7–1·6)
Musculo-skeletal	1345 (88%)	35 (2%)	68 (4%)	76 (5%)	1·12 (0·8–1·6)

Data are number (%) or odds ratio (95% CI). *Defined as a symptom that began after arrival at work. †Pairs of responses within each trial judged to be independent observations.

Table 6: **Matched unadjusted analysis of reported symptoms**

from the same floors or buildings). To assess the possibility of a temporal trend, the effect of UVGI estimated in the last 4 weeks was compared with that in the first 2 weeks.

To provide within-person comparisons of symptoms with UVGI on and off, we used conditional logistic regression adjusted for changing environmental covariates (the PHREG procedure in SAS, version 8).[27] This method analysed every person as a stratum if they completed at least one questionnaire with UVGI on, and one with UVGI off, and had some variation in response. Individuals' characteristics, such as age or sex, were not included, since they could not alter the within-person estimate of effect. Potential building effects, that could cause variations in the adjusted odds ratios, were assessed by adding three interaction terms of condition and building to the regression models. There were too few persons per floor, and no easily available software, to reliably model the degree of floor-to-floor variations with this random effects multivariate conditional logistic regression model. However, the random effects models used in the crude analyses suggested that the degree of heterogeneity in the odds ratio by floor was negligible. To assess potential effect modification by personal or medical characteristics, conditional logistic regression was repeated within subgroups, and by trial.

Role of the funding source

The funding sources, and the manufacturer of the UVGI lamps, had no role in trial design, data collection, data analysis, data interpretation, writing of the manuscript, or the decision to publish these results.

Results

1011 eligible workers were identified, of whom 153 (15%) did not respond, 87 (9%) were classified as dropouts, and 771 (76%) participated (figure 2). On average, participants completed 4·75 symptom questionnaires. Table 1 shows that personal and work characteristics of the three groups did not differ significantly, although little information about non-respondents was available.

At worksites, thermal and chemical indices did not differ by much when UVGI were on compared with when they were off (table 2). However, table 3 shows that on surfaces exposed to UVGI, median concentrations of viable micro-organisms and endotoxins were reduced by an overall average of 99% (95% CI 67–100). Compared with UVGI off, operation of UVGI was associated with much lower airborne microbial and endotoxin concentrations in the supply airstream, a non-significant reduction in airborne bacteria at worksites (table 3), and substantial reduction of five of seven common fungal species identified on surface samples (table 4).

Participants' assessment of thermal, physical, and air-quality indices, adequacy of ventilation, and effect of environmental conditions on their work did not change over the course of the study, and were not different with UVGI on or off (table 5). During the weeks that UVGI was on, building management and ventilation system operators did not receive any complaints or concerns from occupants that could have been related to the UVGI (eg, odours).

With UVGI on, workers reported substantially fewer work-related mucosal, respiratory, and overall symptoms (table 6). Work-related systemic symptoms, as well as

	Any	Systemic	Mucosal	Respiratory	Musculoskeletal
All participants†					
UVGI on *vs* off	0·8 (0·7–0·99)	1·1 (0–9–1·3)	0·7 (0·6–0·9)	0·6 (0·4–0·9)	0·8 (0·6–1·1)
Higher worksite temperature (per °C)	1·1 (1·05–1·2)	1·1 (1·03–1·2)	1·1 (1·0–1·1)	1·0 (0·9–1·1)	1·1 (0·9–1·2)
Higher worksite humidity (per 10%)	0·9 (0·8–1·0)	1·0 (0·9–1·1)	0·9 (0·8–1·0)	1·0 (0·9–1·1)	1·0 (0·9–1·1)
Higher worksite CO_2 (per 50 ppm)	1·1 (1·02–1·15)	1·0 (1·0–1·1)	1·1 (1·0–1·2)	1·0 (1·0–1·1)	1·0 (1·0–1·1)
Within subgroups‡ (odds shown for UVGI on *vs* off)					
Atopic	0·7 (0·5–0·9)	1·1 (0·8–1·5)	0·6 (0·5–0·8)	0·6 (0·3–1·1)	0·7 (0·4–1·1)
Non-atopic	0·9 (0·7–1·2)	1·0 (0·8–1·3)	0·8 (0·6–1·1)	0·6 (0·3–1·2)	0·9 (0·6–1·4)
Women	0·7 (0·5–0·9)	1·0 (0·8–1·2)	0·6 (0·5–0·8)	0·6 (0·3–1·01)	0·8 (0·5–1·1)
Men	1·1 (0·8–1·5)	1·2 (0·9–1·7)	1·0 (0·7–1·3)	0·5 (0·2–0·9)	0·8 (0·5–1·5)
Current smoker	1·1 (0·8–1·6)	1·3 (0·9–1·9)	0·9 (0·7–1·4)	0·7 (0·3–1·5)	1·5 (0·8–2·7)
Ex-smoker	0·7 (0·5–1·01)	1·0 (0·7–14)	0·7 (0·5–0·9)	0·7 (0·3–1·6)	0·7 (0·4–1·3)
Never smoked	0·8 (0·6–1·01)	1·0 (0·8–1·4)	0·7 (0·5–0·9)	0·4 (0·4–0·9)	0·5 (0·3–0·9)

Data are odds ratio (95% CI). *From Matched multivariate analysis using conditional logistic regression). †The following environmental indices, when added to a model including UVGI, temperature, humidity, and CO_2 were not significantly associated with symptoms: worksite nitrogen oxides, TVOCs, formaldehyde, ozone, airborne fungi or bacteria, and HVAC surface bacteria or fungi. ‡Adjusted for temperature, humidity, and CO_2 at worksites.

Table 7: **Within-person subject estimates of effect of UVGI on symptoms, adjusted for environmental covariates measured at work sites***

symptoms that began before work were not very different. After adjustment for work-site environmental covariates, overall, mucosal, and respiratory symptoms were greatly reduced with UVGI on, especially in women, workers with an atopic history, and non-smokers (table 7). The effect of UVGI had a smaller, but still significant, effect in the last 4 weeks of the trial, compared with the first 2 weeks (data not shown).

With a random effects model, the variance of the crude odds ratios across participants was zero. The bootstrap method produced CIs almost identical to those shown in table 6. There was no evidence of heterogeneity of unadjusted or adjusted odds ratios between floors or buildings, which suggests there was no clustering of responses within people, floors, or buildings (data not shown in tables).

Discussion

Use of UVGI lights in central ventilation systems in office buildings resulted in substantial reduction of viable micro-organisms on exposed surfaces, and a large fall in work-related symptoms in 771 participating office workers. Strengths of our work include the simplicity of the intervention, within-person estimates of effect, high response-rate of a large number of workers, blinding, and detailed measurement of environmental covariates. Limitations might be the small number of buildings analysed, non-randomised intervention, low preintervention microbial contamination, modest effect of UVGI on worksite microbial measurements, and little understanding of possible mechanisms for the apparent health benefits.

Experimental investigations are rarely done in office buildings. Barriers to such research include the need to negotiate with building owners, corporate tenants, management, unions and workers, the difficulty in controlling this complex environment, and few practical interventions that can be controlled experimentally. UVGI was chosen as the intervention because it is safe, fairly inexpensive to install, and it could be experimentally controlled while maintaining masking, since office workers do not have access to the central ventilation systems.

Because of the repeated measures design, the effect of UVGI could be estimated within people. This design should have controlled potential bias related to between-person differences in personal and work characteristics that can greatly affect questionnaire interpretation and symptom reporting.[3,4,18,28] The study population included a large number of office workers in various occupations employed by public and private organisations, which should enhance the generalisability of results. Potential selection bias was reduced by the high level of participation; and reporting bias controlled by masking.

Misclassification of exposure, related to spatial and temporal variation of environmental covariates within buildings,[18,29,30] was kept to a minimum by measurement of many environmental indices at multiple worksites, at the same time as questionnaire completion. This was done to enhance the precision of adjustment for these environmental covariates, which are known to affect symptom reporting.[18,19,29,31,32]

Few buildings were studied, which could limit generalisability of results. However, we selected study buildings that had characteristics associated with non-specific building-related illnesses,[3-5] and to be typical of most office buildings in Europe and North America. The study buildings did not have substantial microbial contamination. In buildings with greater HVAC microbial contamination, results might be different, although, intuitively, UVGI might be expected to result in greater benefit.

Symptoms were measured with UVGI off first, because measurement of symptoms before exposure to UVGI could indicate exposure to long-term microbial contamination. Subsequently, the time needed for regrowth of surface microbes with UVGI off, was 3 months compared with less than 3 weeks to eradicate them with UVGI on. If the intervals with UVGI on had been lengthened to make them equal, the resultant 18-month duration of the study would probably have led to more refusals by building management, and more drop-outs or non-responders among workers.

Several findings suggest that the apparent benefit of UVGI was not the artifactual result of an order effect. First, no such effect was seen for work-related systemic symptoms, nor symptoms that began before arrival at work. Second, there was no temporal trend in environmental satisfaction ratings. Third, the improvement was consistently greatest in atopic and non-smoking workers who are more likely to develop immunologically related mucosal, respiratory, and muscular symptoms from microbial antigen exposures.[8,33] Finally, there was no evidence of a temporal trend in reduction of benefit of UVGI over trials.

Although use of UVGI led to a 99% reduction of microbial contamination on exposed surfaces, airborne microbial levels did not fall by much. Several reasons can account for this finding. Amounts of airborne fungi and endotoxins were too low to detect a significant difference, even though such low amounts can affect the health of susceptible individuals.[6,34] Airborne bacteria were reduced by 25–30% with UVGI. The remaining airborne bacteria might have been from local sources, including the workers themselves; these would not be altered by the study intervention.

In view of the modest reduction in worksite airborne concentrations, how could UVGI have led to decreased symptoms? UVGI reduced growth of fungi and bacteria previously associated with sinusitis,[15] asthma,[6,17] humidifier fever,[8,11,12,14] and hypersensitivity pneumonitis[6,11,12] (table 3). Also, endotoxin production was eliminated almost entirely, which has been associated with influenza-like[16] or respiratory[37] symptoms, and changes in lung function.[36,37] An alternate explanation is that UVGI reduced the aerosolisation of microbial antigenic proteins. Unfortunately, these were not measured, but this hypothesis is lent support by the greater benefit from UVGI in non-smokers and workers with an atopic history (who have greater risk for immune reaction to such antigens) than in others.[8,33]

Outbreaks of building-related illnesses are typically discovered when one or more workers present with asthma, or hypersensitivity pneumonitis.[6,11-13] An important, but often overlooked, feature of these outbreaks is that a much larger number of workers have non-specific symptoms[6,11,12] that would have been labelled non-specific building-related symptoms, had it not been for the few severe cases.[3] Those who are more susceptible, such as people with a history of atopy,[3,4] are more affected,[3] which is confirmed by our results, showing that workers with an atopic history had greater reduction in symptoms with UVGI than those with no such history.

Because the first principle of remediation is source control, we tested whether UVGI could reduce symptoms by elimination of an important potential source of microbial contamination.[2] Central air-conditioning systems almost always have microbial contamination,[8,12,13] and epidemiological researchers have consistently linked these systems to building-related symptoms.[4,5] Therefore, the most important interpretation of our work is that microbial

contamination of air conditioning systems is a potentially remediable cause of building-related symptoms in susceptible workers. Since UVGI eliminated almost entirely all surface bacteria, fungi, and endotoxin, the non-specificity of this technology[38] means that it could provide source control without having to first characterise the microbial contaminants.

Extrapolating from our results, UVGI could be installed in most existing office buildings in North America to resolve work-related symptoms due to HVAC microbial contamination in about 4 million workers.[2] To install UVGI in the ventilation systems of an 11 148 m² office building with 1000 occupants would cost US$52 000, and $14 000 per year for energy, maintenance, and bulb replacement (estimates from manufacturer). For every worker, the estimated $52 for initial and $14 for yearly operating costs, compare favourably with the estimated yearly losses from absence caused by building-related sickness.[2]

Contributors

D Menzies, T Rand, J Popa, and D Milton contributed to initial concept, design, and obtaining funding, data collection (including specific laboratory work). D Menzies also drafted and revised the manuscript and, with J Hanley and J Popa, analysed data. J Popa, T Rand, J Hanley, and D Milton critically revised the manuscript.

Conflict of interest statement

None declared.

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